IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application No.	:	09/925,728
Applicants	:	GEISTLICH, et al.
Filed	:	August 10, 2001
TC/A.U.	:	3738
Examiner	:	B.E. Pellegrino
Confirmation No.	:	5552
Docket No.	:	1194-179
Customer No.	:	6449

Title: METHOD FOR PROMOTING REGENERATION OF SURFACE CARTILAGE IN A DAMAGED JOINT

Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

APPELLANT'S BRIEF ON APPEAL UNDER 37 C.F.R. §41.37

Sir:

The following comprises the Applicants' Brief on Appeal from the Office Action dated September 19, 2005, in which claims 1-11, 13-20, and 22 were finally rejected. A Notice of Appeal was filed December 19, 2005. The Commissioner for Patents is authorized to charge Deposit Account No. 02-2135 for the required Appeal fee set forth in 37 C.F.R. § 1.17(c) and a fee and petition for a two-month extension of time extending the time for filing an Appeal Brief to April 19, 2006. Accordingly, this Appeal Brief is being timely filed.

I.

REAL PARTY IN INTEREST

The owner of the above-referenced patent application and the real party in interest in this appeal is the Assignee, Ed. Geistlich Söehne A.G. für chemiche Industrie, located in Wolhusen, Switzerland.

II.
RELATED APPEALS AND INTERFERENCES

The Applicants are unaware of any other appeals or interferences related to the subject matter of this appeal.

III.
STATUS OF CLAIMS

Claims 1-11, 13-20, and 22 are pending and were rejected in the Final Office Action dated September 19, 2005. Claims 12, 21, 23 and 24 had been canceled by previous Amendments. Applicants appeal from the rejection of claims 1-11, 13-20, and 22. The appealed claims are reproduced in the Appendix attached hereto.

IV.
STATUS OF AMENDMENTS

No proposed Amendment subsequent to the outstanding Final Office Action has been filed in this application.

V.
SUMMARY OF THE CLAIMED SUBJECT MATTER

The present invention is directed to methods of promoting regeneration of surface cartilage of a joint, comprising covering an area of damaged cartilage of a joint with a patch consisting essentially of a multilayer sheet of collagen membrane material, fixing the patch over the area without application of a separate hemostatic barrier layer in the area, and allowing the area to regenerate. The methods are useful in repairing injuries and damage to surface cartilage in joints, such as knees (specification at page 2, paragraph [0014]).

In view of the large number of annual joint injuries, such as knee injuries, a number of therapies have been developed in an effort to promote regeneration of damaged cartilage. Methods typically have involved introduction of chondrocytes from an outside source into the damaged area to promote cartilage regeneration. For example, in accordance with one previously known method, a cartilage biopsy is surgically removed from the patient and sent to a laboratory, where the patient's chondrocytes are isolated from the cartilage and the chondrocyte cells are reproduced in culture. Later, another surgery is performed on the patient wherein the damaged cartilage area to be treated is debrided back to expose healthy cartilage, leaving the subchondral bone plate intact. A periosteal patch is taken from the proximal medial tibia of the patient, and this periosteal patch is sutured to the rim of the healthy cartilage surrounding the area to be treated. The cultured chondrocytes reproduced from the cells previously taken from that patient then are injected under the patch into the defect, and the injury is allowed to heal. In another known method, a hemostatic barrier is placed proximal to the surface to be treated, chondrocytes in the matrix are placed upon the surface to be treated distal to the hemostatic barrier, and then the matrix is covered with a patch. There remains a need in the art for improved methods of promoting regeneration of surface cartilage in damaged joints. (Specification, at page 1, paragraphs [0003]-[0006]).

The present invention achieves the desired goals through a novel method of promoting regeneration of surface cartilage of a joint. Independent claim 1 defines this method as including the steps of covering an area of damaged cartilage of a joint to be treated with a patch consisting essentially of a multi layer sheet of collagen membrane material, wherein said multi layer sheet of collagen membrane material is comprised of at least one barrier layer which acts as a barrier to inhibit passage of cells therethrough, wherein said at least one barrier layer has a thickness of about 0.2-2mm and has a structure consisting essentially

of collagen I, collagen III or mixtures thereof, wherein said sheet of collagen membrane material further comprises a matrix layer having a thickness of about 0.2-12mm and having a matrix structure which consists essentially of collagen II having an open sponge like texture; wherein said barrier layer has at least one smooth face so as to inhibit cell adhesion thereon, said barrier layer further having a fibrous face opposite said smooth face, wherein said matrix layer is adhered to said fibrous face; fixing the patch over said area with the at least one said barrier layer oriented away from the damaged area, and said matrix layer with a mixture structure consisting essentially of collagen II oriented toward the damaged area wherein said patch is fixed over the damaged area without application of a separate hemostatic barrier layer in said area; and allowing said area to regenerate cartilage (specification, at page 2, paragraph [0007], page 3, paragraph [0022], page 4, paragraph [0024], page 8, paragraph [0045], Fig. 4A, reference characters 115, 115, 118, and 120). This method is not taught or suggested in the art.

Dependent claim 6 further defines the method of claim 1 wherein the membrane material carries at least one pharmaceutically or biologically active substance or mesenchymal stem cells having the ability to differentiate into cells to regenerate cartilage or bone. Dependent claim 7 further defines the pharmaceutically active substance of intervening dependent claim 6 as being selected from the group consisting Taurolidine, Taurultam and a mixture thereof. (Specification at page 7, paragraph [0037] and originally filed claims 6 and 7).

Dependent claim 22 further defines the at least one barrier layer (of claim 1) as being derived from peritoneum membrane from calves or pigs. (Specification at page 9, paragraph [0048]).

Dependent claim 8 further defines the pharmaceutically active substance of intervening dependent claim 6 as being selected from the group consisting of cell growth promoting hormones, bone morphogenetic proteins (BMPs), other

skeletal matrix molecules, and signaling peptides. Dependent claim 9 further defines the pharmaceutically active substance (of claim 6) as being selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-7, BMP-8, OP-1, PTH, TGF-, TGF-1, VEGF, CIP, IGF, PTHrP, PDGF and mixtures thereof. (Specification at pages 6-7, paragraph [0036]).

Dependent claim 11 further defines the membrane material recited in claim 1 as carrying bone marrow stromal cells. (Specification, at page 7, paragraph [0037]).

Dependent claim 13 further defines the method of claim 1 as comprising implanting a resorbable bone mineral implant material into a region of bone injury in the area to be treated, prior to fixing said patch over said area to be treated. Dependent claim 14 further defines the bone mineral as being charged with chondrocytes. (Specification at page 3, paragraph [0018]).

Dependent claim 17 further defines the patch recited in claim 1 as comprising said matrix layer sandwiched between one said barrier layer and a second said barrier layer. (Specification at page 4, paragraph [0024] and Figure 4A, reference characters 115, 116, 118, and 120).

VI.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following issues are presented by this appeal:

1) Whether claims 1-6, 10, 15, 16, and 18-20 are unpatentable under 35 U.S.C. § 103(a) as obvious over Abdul-Malak, et al. (U.S. Patent No. 5,567,806), in view of Stone, et al. (U.S. Pat. No. 5,624,463).

2) Whether claims 7 and 22 are unpatentable under 35 U.S.C. § 103(a) as obvious over Abdul-Malak, et al. (U.S. Patent No. 5,567,806), in view of Stone,

et al. (U.S. Pat. No. 5,624,463), and further in view of Geistlich, et al. (WO 95/18638).

3) Whether claims 8 and 9 are unpatentable under 35 U.S.C. § 103(a) as obvious over Abdul-Malak, et al. (U.S. Patent No. 5,567,806), in view of Stone, et al. (U.S. Pat. No. 5,624,463), and further in view of Sonis (WO 90/13302).

4) Whether claim 11 is unpatentable under 35 U.S.C. § 103(a) as obvious over Abdul-Malak, et al. (U.S. Patent No. 5,567,806), in view of Stone, et al. (U.S. Pat. No. 5,624,463), and further in view of Caplan, et al. (U.S. Pat. No. 5,197,985).

5) Whether claims 13 and 14 are unpatentable under 35 U.S.C. § 103(a) as obvious over Abdul-Malak, et al. (U.S. Patent No. 5,567,806), in view of Stone, et al. (U.S. Pat. No. 5,624,463), and further in view of Geistlich, et al. (U.S. Pat. No. 5,573,771).

6) Whether claim 17 is unpatentable under 35 U.S.C. § 103(a) as obvious over Abdul-Malak, et al. (U.S. Patent No. 5,567,806), in view of Stone, et al. (U.S. Pat. No. 5,624,463), and further in view of Seid (U.S. Pat. No. 5,254,133).

VII.

ARGUMENT

1) The rejection of claims 1-6, 10, 15, 16, and 18-20, under 35 U.S.C. § 103(a) is improper

In the Final Office Action dated September 19, 2005, the Examiner maintained the rejection of claims 1-6, 10, 15, 16, and 18-20 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Abdul-Malak (U.S. Pat. No. 5,567,806), in view of Stone, et al. (U.S. Pat. No. 5,624,463). Claim 1 is independent and claims 2-6, 10, 15, 16, and 18-20 all depend therefrom. As noted above, the present invention is directed to, *inter alia*, a method of

promoting regeneration of surface cartilage of a joint, comprising: covering an area of damaged cartilage of a joint to be treated with a patch consisting essentially of a multi layer sheet of collagen membrane material, wherein said multi layer sheet of collagen membrane material is comprised of at least one barrier layer which acts as a barrier to inhibit passage of cells therethrough, wherein said at least one barrier layer has a thickness of about 0.2-2mm and has a structure consisting essentially of collagen I, collagen III or mixtures thereof, wherein said sheet of collagen membrane material further comprises a matrix layer having a thickness of about 0.2-12mm and having a matrix structure which consists essentially of collagen II having an open sponge like texture; wherein said barrier layer has at least one smooth face so as to inhibit cell adhesion thereon, said barrier layer further having a fibrous face opposite said smooth face, wherein said matrix layer is adhered to said fibrous face; fixing the patch over said area with the at least one said barrier layer oriented away from the damaged area, and said matrix layer with a mixture structure consisting essentially of collagen II oriented toward the damaged area wherein said patch is fixed over the damaged area without application of a separate hemostatic barrier layer in said area; and allowing said area to regenerate cartilage. Thus, the method of the present invention utilizes a multilayer collagen membrane that includes an impermeable barrier layer and a porous matrix layer, each layer type performing different functions in the ultimate promotion of tissue regeneration in a joint. As Applicants' specification states, "[a]s a material for guided tissue regeneration, cell growth is encouraged by the matrix layer. The barrier layer inhibits undesired cell growth." (specification, paragraph [0063]). Furthermore,

> "[w]hile not wishing to be bound by theory, it is now believed that successful cartilage regeneration requires that the rapid ingrowth not only of native tissue cells, such as connective tissues, blood vessels etc., but also of any new bone tissue into the site of the defect be prevented. This may be achieved using a double-layer

membrane in accordance with the invention which serves to shield the collagen matrix from the ingrowth of native tissue cells from one side."
[0029]

Therefore, the barrier layer, which is specially adapted to be adhered to the matrix layer, serves a vital role in the ultimate success of the claimed tissue regeneration method, by performing a function that essentially serves as a check on the ingrowth encouraged by the matrix layer. Native cells therefore are unable to penetrate or grow into the barrier layer.

The present invention avoids the necessity of providing a separate hemostatic barrier as in U.S. Patent No. 5,759,190, a separate chondrocyte-charged matrix placed distal to the hemostatic barrier as described therein, and a separate patch covering the matrix as in said patent. (See paragraph [0021]).

Thus, the patch utilized in the methods of the present invention includes at least one barrier layer that consists essentially of collagen I or collagen III (or a mixture thereof), and, adhered thereto, a matrix layer having a matrix structure consisting essentially of collagen II. The barrier layer inhibits passage of cells therethrough, while the matrix layer does the opposite, with its open, sponge-like texture. The barrier has a smooth face and a fibrous face, the smooth face inhibiting cell adhesion and the matrix being adhered to the fibrous face. In the claimed methods, the barrier is oriented away from the damaged area and the matrix is oriented toward the damaged area. Thus, the method employs a multilayer patch, each of the layers being specifically oriented, consisting essentially of particular materials, and each performing a particular function. As noted below, the art of record does not teach or suggest a method utilizing a patch having such features.

According to the Examiner, Abdul-Malak, et al. discloses a method of promoting tissue regeneration through the use of a collagen membrane that can

be sutured at the site of repair, and a multilayer membrane that can be crosslinked, having different layers of collagen that can be used in the method. According to the Examiner, Abdul-Malak additionally discloses that the collagen membrane can be impregnated with glycosaminoglycan, which can be hyaluronic acid, and that the collagen used can be collagen I or III. The Examiner further stated that "[i]t can be construed that Abdul-Malak disclose a matrix layer is oriented toward the damaged area since the membrane is a texture, i.e. 'sponge-like' for tissue ingrowth, col. 2, lines 41-44, col. 6, lines 5-9." (September 19, 2005 Final Office Action, page 2). The Examiner acknowledged that "Abdul-Malak et al. do not disclose using collagen II as one of the layers in joint repair or that bonding can be used to fix the membrane at the site or to use cartilage cells, such as condorcytes [sic] with the membrane." (September 19, 2005 Final Office Action, page 2).

The Examiner has taken the position that Stone shows, in Figure 9, a barrier layer 12 oriented away from the damaged area in a cavity of a joint and that such barrier can be made predominantly of collagen I (col. 7, lines 56,57). Specifically, the Examiner stated that

> "[i]t can also be interpreted that the barrier layer 12 has a fibrous face and smooth face as shown (Fig. 9) for adhering to the inner material, col. 9, lines 62,63, col. 10, lines 1,2. The examiner is interpreting the claimed elements 'barrier layer' in this way: since the outer material of Stone is a boundary, it can be construed as a barrier layer. Claims in a pending application should be given their broadest reasonable interpretation." (September 19, 2005 Final Office Action, pages 2-3).

The Examiner asserted that Stone also shows the multi-component patch device has the inner component with an open sponge-like texture, Fig. 4B. The Examiner asserted that Stone additionally teaches the inner material is also made of collagen and can be collagen II, (col. 9, lines 33-35, col. 12, lines 54-56). The

Examiner stated that for purposes of applying prior art under 35 U.S.C. §103, since there is no clear indication in the specification or claims (in the Examiner's opinion), of what the basic and novel characteristics actually are, the term "consisting essentially of" will be construed as equivalent to "comprising." Moreover, the Examiner stated that Stone teaches that the patch or device is fixed to the area of treatment by adhesively bonding to the area, that biologically active substances, such as chondrocytes, are charged into the patch, and that Stone also teaches that natural cartilage from pigs can be used to obtain collagen II, which the Examiner asserted to be inherently hyaline type. The Examiner concluded that it would have been obvious to one of ordinary skill in the art to substitute collagen II with chondrocytes, as taught by Stone, in the membrane of Abdul-Malak, such that it provides a natural material present in the area that it is used for, such as collagen II (which the Examiner stated is commonly present in cartilage). The Examiner asserted that, regarding the thickness limitations, it would have been an obvious matter of design choice to modify the thickness of the barrier layer or matrix layer, since, in the Examiner's view, Applicant has not disclosed that using the specific thickness for each layer provides any advantage, or solves a stated problem, or is chosen for any particular purpose. The Examiner further asserted that one of ordinary skill in the art would have expected Applicant's invention to perform equally well with the thickness of the layers taught by Abdul-Malak or the claimed 0.2-2mm for the barrier layer or the 0.2-12mm for the matrix layer in claim 1 because both membranes perform the same function of utilizing collagen as the repair material.

In response to the Examiner's various contentions, for at least the reasons stated below, Applicants respectfully submit that the rejection of claims 1-6, 10, 15, 16, and 18-20 is improper under 35 U.S.C. §103. In short, there is no motivation to combine the Abdul-Malak, and Stone references as the Examiner has done, and, moreover, even if combined, the combination would fail to teach

all of the limitations of the rejected claims. Simply put, the art cited by the Examiner in rejecting the claims, taken either alone or in combination, neither teaches nor suggests Applicants' claimed method of promoting regeneration of surface cartilage of a joint.

All of the Examiner's rejections rely on a combination of Abdul-Malak in view of Stone. Abdul-Malak refers generally to a biocompatible slow-resorbing membrane which can be used in guided tissue regeneration, and methods of its manufacture. The membranes referred to in Abdul-Malak, however, differ from the membranes used in Applicants' claimed methods in various ways. Applicants' invention involves use of a multilayer sheet of collagen membrane material, having at least one barrier layer that acts as a barrier to inhibit passage of cells therethrough, wherein the barrier layer has a structure consisting essentially of collagen I, collagen III or mixtures thereof. The membrane utilized in the present invention further comprises a matrix layer having a matrix structure which consists essentially of collagen II, having an open sponge like texture. The barrier layer has at least one smooth face to inhibit cell adhesion thereon, and a fibrous face opposite the smooth face, the matrix layer being adhered to said fibrous face. As pointed out in Applicant's specification, a basic feature of the Applicants' invention and one that serves as a distinction over the prior art, is its use of a multilayer membrane having individual matrix and barrier components that are formed of different materials and that serve different functions. Significantly, this is achieved without the need to employ a separate (i.e., separated or apart) barrier. In contrast, the membranes referred to in Abdul-Malak are wholly porous, having no barrier layer of any sort. Indeed, there is no suggestion that any such individual barrier layer could, or desirably should be adhered to a matrix layer for any purpose, let alone purposes provided in the present invention, such as to inhibit passage of cells therethrough. Abdul-Malak does not recognize what Applicants have, that too much ingrowth can be

undesirable and counterproductive in tissue regeneration and thus should be inhibited. Thus, Abdul-Malak has not suggested the desirability of a membrane of the type used in Applicants' claimed methods. Moreover, as Examiner has acknowledged, the matrix of Abdul-Malak may be type I or type III collagen, but there is no suggestion that a matrix can consist essentially of type II collagen. Furthermore, Applicants' claimed invention is directed to, *inter alia*, methods for promoting regeneration of surface cartilage of a joint, whereas Abdul-Malak makes no mention of joint damage or repair. Rather, the membranes of Abdul-Malak, are described only as being suited for periodontal use. Therefore, Abdul-Malak makes no mention of the claimed use of the present invention (promoting regeneration of surface cartilage of a joint), no mention of any barrier layer at all, let alone one having a smooth and a fibrous face, each performing a unique function, and no mention of the use of type II collagen in a matrix structure. The Examiner correctly notes that Abdul-Malak refers to a membrane having at least two layers (col. 2), but fails to recognize that the same discussion in the reference indicates that both layers are porous matrix layers. The Examiner even notes the sponge-like appearance for tissue ingrowth. The Abdul-Malak patent in fact notes that "the above-mentioned membrane", that is, the two-layered matrix, "is made porous to have a sponge-like appearance." (col. 2, lines 41-44). Thus, no matter how many collagen layers are used in a membrane described in the Abdul-Malak reference, it is clear that the entire membrane is made of a porous matrix structure whose function is to encourage tissue growth. There is no hint or suggestion of the need or desirability of an additional, barrier layer that serves to inhibit cell growth therethrough.

The Examiner has relied on Stone to cure the various deficiencies of Abdul-Malak described above.

As stated in MPEP§2143:

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Motivation can come from the "nature of the problem to be solved, the teachings of the prior art, [or] knowledge of persons of ordinary skill in the art." In *re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). See also MPEP §2143.01, which further notes that in *In re Fulton*, 391 F.3d 1195, 73 USPQ2d 1141 (Fed. Cir. 2004), the court emphasized that the proper inquiry is "whether there is something in the prior art as a whole to suggest the *desirability*, and thus, the obviousness, of making the combination."

The §103 rejections on appeal are improper because they fail to establish a *prima facie* case of obviousness. The cited art does not disclose or suggest all elements of the rejected claims, and, moreover, no motivation exists to combine the cited references as the Examiner has suggested.

As noted above, Abdul-Malak refers to a porous matrix for use in regeneration of tissue in periodontal applications. Stone refers to a device for use in other applications, such as joints, that includes a porous matrix attached to an inner base component for securing the matrix to an underlying bone. Both refer to matrices that are porous and made of Type I or III collagen and perform the function of allowing and/or encouraging tissue growth therethrough.

First, Applicants take the position that one of ordinary skill in the art would not be motivated to add the matrix structure of Stone, used in articular bone applications, to the matrix structure of Abdul-Malak, used in periodontal

applications, because doing so would amount to adding nothing more than another porous structure for tissue ingrowth to Abdul-Malak's already similar porous matrix structure for tissue ingrowth. No apparent advantage would be gained from such an addition.

Furthermore, Applicants note the Examiner's assertion that Stone discloses a "barrier" (component 12 in the figures of Stone) as recited in Applicants' claims. As discussed in more detail below, the Examiner is incorrect in this assertion. If, however, Stone did indeed suggest such a structure (which it does not) that had tissue growth inhibition qualities comparable to Applicants' barrier layer, there still would have been no motivation to modify the device of Abdul-Malak with such a component. The art simply does not recognize any advantage that could be gained by inhibiting tissue from growing into the matrix, rather than encouraging it. Therefore, the obviousness rejection is improper for at least the reason that there is no motivation for one of ordinary skill in the art to combine the references as the Examiner has suggested, regardless of the various interpretations that the Examiner might assign to the reference teachings. Furthermore, given the more than two dozen known collagen types, found in various different tissues, one would have had no reasonable expectation that one could successfully replace a type useful in Abdul-Malak's periodontal applications with a different type which is useful in Stone's articular bone applications.

Perhaps more significantly, however, even if the reference teachings were combined, the combination simply would not result in Applicants' claimed invention, because no combination of the cited references teaches or suggests all limitations of Applicants' claims. In particular, no combination of Abdul-Malak and Stone yields a barrier layer as recited in Applicants' claims. Stone refers generally to a prosthetic device having two main components—a "base component" and a matrix. The matrix of Stone is defined (col. 3 lines 7-24) as being a "dry, porous volume matrix" that "establishes a bioresorbable scaffold

adapted for the ingrowth of articular chondrocytes." (The base component is a structure that has no analogous component in either the Abdul-Malak device or Applicants' claimed invention.)

According to the description provided in the Stone patent, (col. 3, lines 56-62), "[a] generally conical, biocompatible base component extends away from one base of the matrix for use in insertion and anchoring of the matrix to an underlying bone." The figures are consistent with this description and clearly depict the base component as oriented toward the defect in the bone and the matrix oriented away from the defect. It is also clear from both the description and drawings that the base component cannot reasonably be interpreted as being a "membrane" or forming part of a "membrane." The device of Stone appears to require the use of the base component structure to anchor the matrix to the bone to achieve the function of cartilage tissue regeneration. (See, e.g., column 5, lines 53-56). The Stone patent, throughout its description, refers to the matrix and base component as being distinct structures performing these particular functions. For example, the paragraph bridging cols. 5 and 6 describes this supportive role for the base component and states that the base component "may function in this supportive capacity until sufficient tissue ingrowth occurs in the matrix 12 to then provide that function." The description goes on to state that the fibers that make up the matrix "can provide mechanical strength and protection and lubrication while encouraging tissue ingrowth." While this encouragement of tissue growth is a comparable function to that of the differently oriented matrix layer of Applicants' multilayer membrane, it is the opposite function of the Applicants' barrier layer. Such a conclusion is again clearly supported at cols. 9 and 10 of Stone, which describe the matrix itself (not any additional barrier) as being connected to the base component. Table 1 similarly makes clear that the base component and matrix are separate, distinct structures, albeit attached to each other as described elsewhere. The Stone device thus includes a base

component anchoring a matrix that promotes tissue regeneration. There is no additional barrier layer adhered to the matrix. The matrix in Stone is simply that—a matrix. It is not and cannot be construed as both a matrix and a barrier layer.

Despite the above clear teachings of Stone, the Examiner has attempted to shoehorn the matrix of Stone into Applicants' definition of a barrier layer, based solely on the observation that the location (not function) of Stone's matrix layer renders it the "outer material" of Stone's device and thus "a boundary" or, in the Examiner's view, a "barrier." (See Final Office Action, page 3). While in the abstract, this matrix might possibly be regarded as some sort of boundary as the Examiner has postulated, it clearly is not the "barrier layer" of Applicants' invention and cannot reasonably be interpreted to be such. Applicants point out that the Examiner has offered no suggestion whatsoever as to what the matrix of Stone might provide a barrier against. Moreover, Applicants believe that the Examiner's recognition that Stone's matrix is the "outer" material of the device in fact undermines the Examiner's position that Stone's matrix is oriented in the manner specified by Applicants' claims. Applicants' claims require that the matrix be oriented toward the damaged area, not away from it, as in Stone's "outer material" matrix.

Applicants do note that Stone refers at column 6, lines 51-61, to its matrix alternatively having intra- and interfibrillary spaces that slow the rate of cell ingrowth as compared to matrices having wider spaces for more rapid tissue ingrowth. Thus, Stone describes alternate matrices allowing for rapid or, alternatively, less rapid rates of tissue regeneration. Applicants point out, however, that even if one were to construe such a matrix as having some aspects of function comparable to that of the barrier layer of Applicants' invention, it is clear that Stone still would not be describing or suggesting a multilayer membrane having a matrix layer performing one function and a barrier layer

performing an opposite function. There still would only be a single, sponge-like matrix, (albeit having diminished ingrowth capacity), but there would remain no additional barrier layer component. Accordingly, no matter how one combined the teachings of Stone with those of Abdul-Malak, (if such combination is in fact possible), one could not arrive at the membrane utilized in Applicants' claimed method. Such a combination would not and could not include at least the barrier layer required of Applicants' claims.

Furthermore, it should be noted that the base component of Stone, i.e., the part of the system secured to the bone, clearly is not the matrix recited in the Applicants' claims but rather an anchoring structure used to temporarily support a matrix, so that the matrix can perform its stated function of tissue regeneration. Thus in all circumstances presented in Stone, the matrix is oriented away from the damaged bone, while the "base component" is oriented toward it. Thus, for at least the reasons provided above, the prior art cited by the Examiner fails to disclose or suggest all limitations of Applicants' claims, and therefore fails to justify the rejection of claims 1-6, 10, 15, 16, and 18-20 under 35 U.S.C. §103.

Finally, certain elements of Applicants' claimed invention are preceded by "consisting essentially of" transitional language. As noted in MPEP §2111.03, such language limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original). As Applicants have noted, and as the specification sets forth, a feature of the invention that is both basic and novel is its use of a multilayer collagen membrane that includes an impermeable barrier layer and a porous matrix layer, each layer type performing different functions in the ultimate promotion of tissue regeneration in a joint. Desired cell growth is encouraged by the matrix layer, while undesired cell growth is inhibited by the

barrier layer. Adding the additional components provided in the cited references, as the Examiner has done, would alter these characteristics.

All of the claims of the present application specifically recite a multi-layer sheet of collagen membrane material including a smooth-faced barrier layer consisting essentially of collagen I, collagen III or mixtures thereof oriented away from a damaged area, and a matrix layer having a matrix structure consisting essentially of collagen II oriented toward a damaged area. Changing the compositions, orientations and functions of the layers of the membrane used in Applicants' methods would alter the membrane's usefulness and ability to achieve the promotion and regeneration of joint surface cartilage.

In that regard, Abdul-Malak discloses only a Type I or III collagen membrane. While the Examiner asserts otherwise, Stone never teaches or even remotely suggests orienting a matrix layer having a matrix structure consisting essentially of collagen II toward a damaged area. In fact, whenever Stone utilizes collagen II as an "inner material", the collagen II must be combined with hydroxyapatite or tricalcium phosphate (TCP), *See, e.g.*, column 9, lines 32-34, or Example 4.

Clearly, as noted above, the "inner material" of Stone cannot be a matrix structure consisting essentially of collagen II, since the "inner material" is a "conical, rigid base component 20 which extends downward from the underside of matrix 12" (column 5, lines 48-49). From the Stone teaching it is clear that when the "rigid base component 20" contains collagen II, the component must consist essentially of collagen II and TCP or hydroxyapatite, so that the base component can be "compressed" into a "rigid base component 20" (column 13, line 7-9).

Nothing in the combined references suggests orienting a matrix layer with a matrix structure "consisting essentially of collagen II" toward a damaged area, in combination with the other elements of the present claims.

Accordingly, for at least the reasons provided above, Applicants respectfully submit that the rejection of claims 1-6, 10, 15, 16, and 18-20 under 35 U.S.C. §103 is improper and should be reversed.

2) The rejection of claims 7 and 22 under 35 U.S.C. § 103(a) is improper

In the September 19, 2005 Final Office Action, the Examiner maintained the rejection of claims 7 and 22 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Abdul-Malak '806 in view of Stone, et al. '463 as applied to claims 1 and 6 above, and further in view of Geistlich et al. (WO 95/18638). Claims 7 and 22 both ultimately depend from claim 1. The Examiner referred to the application of Abdul-Malak, as modified by Stone, (discussed above in connection with the rejection of claim 1). The Examiner acknowledged, however, that Abdul-Malak in view of Stone does not disclose a pharmaceutical, such as taurolidine, and, does not disclose that the membrane material is taken from the peritoneum. The Examiner stated that Geistlich teaches that chemotherapeutics such as taurolidine can be used with a membrane in cartilage repair, and that Geistlich also teaches the membrane material can be obtained from the peritoneal membranes of calves. The Examiner concluded that it would have been obvious to one of ordinary skill in the art to use the taurolidine or peritoneal material as taught by Geistlich with the method and device of Abdul-Malak as modified by Stone such that it therapeutically treats the patient, and, is from a biological source.

Applicants respectfully submit that the rejection of claims 7 and 22 is improper under 35 U.S.C. §103. The cited art neither teaches nor suggests the methods defined by Applicants' claims. Notwithstanding whether or not Geistlich refers to the use of therapeutics with a peritoneal membrane in cartilage repair, Geistlich fails to supply any of the above-noted deficiencies of the

combination of Abdul-Malak and Stone. Applicants' claimed method is not taught or suggested in the combination of Abdul-Malak and Stone for all of the reasons set forth above in connection with claims 1-6, 10, 15, 16, and 18-20. Thus, because independent claim 1 (from which claims 7 and 22 depend) is not taught or suggested in the art, dependent claims 7 and 22 are similarly not taught or suggested in the art and a rejection of claims 7 and 22 under 35 U.S.C. §103 is therefore similarly improper and should be reversed.

3) The rejection of claims 8 and 9 under 35 U.S.C. § 103(a) is improper

Claims 8 and 9 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Abdul-Malak '806 in view of Stone '463 as Examiner applied those references to claim 6, and further in view of Sonis (WO 90/13302). Claims 8 and 9 both depend from claim 6 and, ultimately, from claim 1. The Examiner referred to the reasoning set forth above with respect to the modification of Abdul-Malak by Stone. The Examiner acknowledged, however, that Abdul-Malak, in view of Stone, does not disclose the membrane carrying pharmaceutically active substances, such as BMP's. The Examiner asserted that Sonis teaches that BMP's can be used with membranes for tissue regeneration, and thus, alleged it would have been obvious to one of ordinary skill in the art to impregnate the membrane with a pharmaceutically active substance, as taught by Sonis, in the membrane of Abdul-Malak, as modified by Stone, in order to enhance the capabilities of the tissue regeneration process and allow for controlled release of the substances.

Applicants respectfully submit that the rejection of claims 8 and 9 is improper under 35 U.S.C. §103. The cited art neither teaches nor suggests the methods defined by Applicants' claims. Notwithstanding whether or not Sonis

refers to the use of BMP's with membranes for tissue regeneration, Sonis fails to supply any of the above-noted deficiencies of the combination of Abdul-Malak and Stone. Applicants' claimed method is not taught or suggested in the combination of Abdul-Malak and Stone for all of the reasons set forth above in connection with claims 1-6, 10, 15, 16, and 18-20. Thus, because independent claim 1 (from which claims 8 and 9 depend) is not taught or suggested in the art, dependent claims 8 and 9 are similarly not taught or suggested in the art and a rejection of claims 8 and 9 under 35 U.S.C. §103 is therefore similarly improper and should be reversed.

4) The rejection of claim 11 under 35 U.S.C. § 103(a) is improper

Claim 11, directed to the method of claim 1, wherein the membrane material carries bone marrow stromal cells, was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Abdul-Malak '806 in view of Stone '463 as the Examiner applied those references to claim 1, and further in view of Caplan, et al. (U.S. Pat. No. 5,197,985). The Examiner referred to the reasoning set forth above with respect to the modification of Abdul-Malak by Stone. The Examiner acknowledged, however, that Abdul-Malak, in view of Stone, does not disclose the use of bone marrow stromal cells incorporated in the membrane. The Examiner asserted that Caplan, et al. teaches that bone marrow cells can be incorporated into carriers or membranes for tissue regeneration and that the stem cells are capable of determining which connective tissue to regenerate. The Examiner stated that the cells and carrier in Caplan are used to repair cartilage of a joint. The Examiner also asserted that Caplan additionally teaches that stromal cells from bone marrow can be harvested for use. The Examiner thus concluded that it would have been obvious to one of ordinary skill in the art to impregnate the

membrane of Abdul-Malak, in view of Stone, with stromal cells as taught by Caplan, et al., in order to provide enhanced osteogenic activity.

Applicants respectfully submit that the rejection of claim 11 is improper under 35 U.S.C. §103. The cited art neither teaches nor suggests the methods defined by Applicants' claims. Notwithstanding whether or not Caplan refers to the incorporation of bone marrow cells into carriers or membranes for tissue regeneration, Caplan fails to supply any of the above-noted deficiencies of the combination of Abdul-Malak and Stone. Applicants' claimed method is not taught or suggested in the combination of Abdul-Malak and Stone for all of the reasons set forth above in connection with claims 1-6, 10, 15, 16, and 18-20. Thus, because independent claim 1 (from which claim 11 depends) is not taught or suggested in the art, dependent claim 11 is similarly not taught or suggested in the art and a rejection of claim 11 under 35 U.S.C. §103 is therefore similarly improper and should be reversed.

5) The rejection of claims 13 and 14 under 35 U.S.C. § 103(a) is improper

Claims 13 and 14 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Abdul-Malak '806 in view of Stone '463 as the Examiner applied those references to claim 1 above, and further in view of Geistlich, et al. (U.S. Pat. No. 5,573,771). Claims 13 and 14 both ultimately depend from claim 1. The Examiner referred to the reasoning set forth above with respect to the modification of Abdul-Malak by Stone. The Examiner acknowledged, however, that Abdul-Malak, in view of Stone, does not disclose the use of a bone mineral implanted in the region of the bone injury. The Examiner asserted that Geistlich et al. '771 teaches that a bone mineral is useful for implanting in a bone cavity for remodeling. According to the Examiner, Geistlich '771 also teaches that the bone

mineral improves strength of the bone at the defect and that these implants can be charged with bone cells. According to the Examiner, it therefore would have been obvious to one of ordinary skill in the art to use a bone mineral as taught by Geistlich, et al. '771 charged with the chondrocytes in the membrane of Abdul-Malak, in view of Stone, in order to strengthen the area of the defect and provide a more natural environment for the cells.

Applicants respectfully submit that the rejection of claims 13 and 14 is improper under 35 U.S.C. §103. The cited art neither teaches nor suggests the methods defined by Applicants' claims. Notwithstanding whether or not Geistlich '771 refers to the use of a bone mineral for implanting into a bone cavity for remodeling, Geistlich '771 fails to supply any of the above-noted deficiencies of the combination of Abdul-Malak and Stone. Applicants' claimed method is not taught or suggested in the combination of Abdul-Malak and Stone for all of the reasons set forth above in connection with claims 1-6, 10, 15, 16, and 18-20. Thus, because independent claim 1 (from which claims 13 and 14 depend) is not taught or suggested in the art, dependent claims 13 and 14 are similarly not taught or suggested in the art and a rejection of claims 13 and 14 under 35 U.S.C. §103 is therefore similarly improper and should be reversed.

6) The rejection of claim 17 under 35 U.S.C. § 103(a) is improper

Claim 17, directed to the method of claim 1, wherein the patch comprises the matrix layer sandwiched between one barrier layer and a second barrier layer, was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Abdul-Malak '806 in view of Stone '463 as the Examiner applied those references to claim 1, and further in view of Seid (U.S. Pat. No. 5,254,133). The Examiner referred to the reasoning set forth above with respect to the modification of Abdul-Malak by Stone. The Examiner acknowledged, however, that Abdul-Malak

in view of Stone do not disclose the use of two barrier layers to sandwich the matrix. The Examiner asserted that Seid teaches in Figure 13, that a coating 76 forms a barrier layer that sandwiches an inner component of the tissue patch. According to the Examiner, Seid also teaches the coating prevents tissue formation, and has referred to col. 9, lines 3-8 to support this assertion. According to the Examiner, therefore, it would have been obvious to one of ordinary skill in the art to use a barrier layer on both sides of the matrix of Abdul-Malak as modified by Stone using the teaching of Seid to inhibit tissue formation prematurely.

Applicants respectfully submit that the rejection of claim 17 is improper under 35 U.S.C. §103. The cited art neither teaches nor suggests the methods defined by Applicants' claims. The Seid reference cited by the Examiner fails to supply any of the above-noted deficiencies of the combination of Abdul-Malak and Stone. Applicants reiterate that Applicants' claimed method is not taught or suggested in the combination of Abdul-Malak and Stone for all of the reasons set forth above in connection with claims 1-6, 10, 15, 16, and 18-20. The Examiner has relied on Seid for its purported teaching of a "barrier" layer (which, in Seid is a coating) that sandwiches an "inner component" of a patch.

First, Applicants respectfully point out that the disclosure of Seid has nothing whatsoever to do with methods of promoting regeneration of surface cartilage of a joint, nothing whatsoever to do with the use of a multilayer sheet of collagen membrane material, and nothing whatsoever to do with a barrier layer which acts as a barrier to inhibit the passage of cells therethrough. Furthermore, Seid makes no mention of collagen types I, II or III. Rather, Seid relates to a surgical implantation device for the repair of hernial ruptures. One of ordinary skill in the art clearly would not even consider Seid in combination with the other art cited by the Examiner because it would appear to have no relevance to promoting regeneration of surface cartilage. Moreover, it is not clear how one

could combine the Seid teachings with those of Abdul-Malak and Stone. However, if such combination were possible, one of ordinary skill in the art would have had no reasonable expectation that Seid's "coating" for use in hernial rupture repair would or could be successfully used in performing the vital role that the Applicants' barrier layers perform in Applicants' claimed methods. Moreover, Applicants note the Examiner's reference to column 9, lines 3-8 of Seid, and its smooth coating "which discourages the formation of scar tissue and prevents the intestine from clinging to the implantation device before tissue has had a chance to grow over it." Notwithstanding the Examiner's assertions, Seid's coating does not perform the function of Applicants' barrier layers, i.e. it does not act "as a barrier to inhibit passage of cells therethrough," as Applicants' claim 1 recites. Moreover, the coating of Seid does not "sandwich" a matrix layer, as required by Applicants' claim 17, but rather, as Examiner has indeed acknowledged, sandwiches merely "an inner component of the tissue patch." (See September 19, 2005 Final Office Action, page 6). The "inner component" of Seid's device, as shown in Figure 13, on which the Examiner has relied, and as described at column 8, lines 44-66, is a "locating member 66 that extends between the first planar member and the second planar member" and "is connected to each of the members by a hook-and-loop fastening mechanism," such as VELCRO. This "inner component" clearly bears no resemblance in either function or design, to the matrix layer of the patch used in Applicants' claimed methods and it clearly is not a matrix "adhered to [a] fibrous face" of a barrier layer of the type recited in Applicants' claims.

Therefore, for the reasons set forth above, a combination of Abdul-Malak, Stone and Seid fails to render obvious claim 17 of Applicants' claimed invention. Accordingly, the rejection of claim 17 under 35 U.S.C. §103 is improper and should be reversed.

In light of the above comments, the Honorable Board is therefore respectfully requested to reverse all grounds of rejection and to direct the passage of this application to issue.

Please charge any fee or credit any overpayment pursuant to 37 CFR 1.16 or 1.17 to Deposit Account No. 02-2135.

Respectfully submitted,

By: 

Patrick T. Skacel
Attorney for Applicants
Registration No. 47,948
ROTHWELL, FIGG, ERNST & MANBECK, p.c.
1425 K Street NW, Suite 800
Washington, DC 20005
Telephone: (202) 783-6040

VIII.
APPENDIX OF CLAIMS ON APPEAL

1. A method of promoting regeneration of surface cartilage of a joint, comprising:

covering an area of damaged cartilage of a joint to be treated with a patch consisting essentially of a multi layer sheet of collagen membrane material, wherein said multi layer sheet of collagen membrane material is comprised of at least one barrier layer which acts as a barrier to inhibit passage of cells therethrough, wherein said at least one barrier layer has a thickness of about 0.2-2mm and has a structure consisting essentially of collagen I, collagen III or mixtures thereof, wherein said sheet of collagen membrane material further comprises a matrix layer having a thickness of about 0.2-12mm and having a matrix structure which consists essentially of collagen II having an open sponge like texture; wherein said barrier layer has at least one smooth face so as to inhibit cell adhesion thereon, said barrier layer further having a fibrous face opposite said smooth face, wherein said matrix layer is adhered to said fibrous face;

fixing the patch over said area with the at least one said barrier layer oriented away from the damaged area, and said matrix layer with a mixture structure consisting essentially of collagen II oriented toward the damaged area wherein said patch is fixed over the damaged area without application of a separate hemostatic barrier layer in said area; and

allowing said area to regenerate cartilage.

2. The method of claim 1, wherein said barrier layer, said matrix layer or both, are impregnated with glycosaminoglycan.

3. The method of claim 2, wherein the glycosaminoglycan is hyaluronic acid, chondroitin 6 sulphate, keratin sulphate or dermatan sulphate.

4. The method of claim 1 wherein the patch is fixed over the area to be treated by adhesively bonding the patch to cartilage surrounding said area to be treated.

5. The method of claim 1 wherein the patch is fixed over the area to be treated by suturing the patch to cartilage surrounding said area to be treated.

6. The method of claim 1 wherein said membrane material carries at least one pharmaceutically or biologically active substance or mesenchymal stem cells having ability to differentiate into cells to regenerate cartilage or bone.

7. The method of claim 6 in which the pharmaceutically active substance is selected from the group consisting Taurolidine, Taurultam and a mixture thereof.

8. The method of claim 6 in which the pharmaceutically active substance is selected from the group consisting of cell growth promoting hormones, bone morphogenetic proteins (BMPs), other skeletal matrix molecules, and signaling peptides.

9. The method of claim 6 wherein the pharmaceutically active substance is selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-7, BMP-8, OP-1, PTH, TGF-, TGF-1, VEGF, CIP, IGF, PTHrP, PDGF and mixtures thereof.

10. The method of claim 1 wherein said membrane material carries articular cartilage stem cells or bone stem cells.

11. The method of claim 1 wherein said membrane material carries bone marrow stromal cells.

12. (Canceled)

13. The method of claim 1 further comprising implanting a resorbable bone mineral implant material into a region of bone injury in the area to be treated, prior to fixing said patch over said area to be treated.

14. The method of claim 13, wherein said bone mineral is charged with chondrocytes.

15. The method of claim 1, wherein said patch is charged with chondrocytes.

16. The method of claim 1 wherein said patch is comprised of a single barrier layer.

17. The method of claim 1 wherein said patch comprises said matrix layer sandwiched between one said barrier layer and a second said barrier layer.

18. The method of claim 1 wherein the matrix layer is provided by collagen II material derived from natural cartilage.

19. The method of claim 18 wherein the collagen II material is derived from hyaline cartilage from pigs.

20. The method of claim 18 wherein the collagen II material is physically cross linked.

21. (Canceled)

22. The method of claim 1 wherein said at least one barrier layer is derived from peritoneum membrane from calves or pigs.

23. (Canceled)

24. (Canceled)

IX.

EVIDENCE APPENDIX

INTENTIONALLY LEFT BLANK

X.

RELATED PROCEEDINGS APPENDIX

INTENTIONALLY LEFT BLANK

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

	Complete if Known
Application Number	09/925,728
Filing Date	August 10, 2001
First Named Inventor	GEISTLICH et al.
Examiner Name	B.E. Pellegrino
Group Art Unit	3738
Attorney Docket Number	1194-179
Total Number of Pages in This Submission 33	Confirmation Number 5552

ENCLOSURES *(check all that apply)*

- [X] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s)
  - [ ] Landscape Table on CD

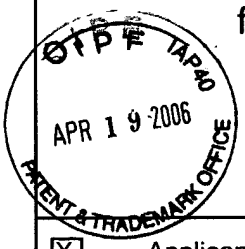
REMARKS:

- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [X] Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) *(please identify below)*:

SUBMITTED BY				Complete (if applicable)	
NAME AND REG. NUMBER	Patrick T. Skacel, Reg. No. 47,948				
SIGNATURE		DATE	April 19, 2005	DEPOSIT ACCOUNT USER ID	02-2135

FEE TRANSMITTAL
for FY 2005

(Small Entity)



Complete if Known	
Application Number	09/925,728
Filing Date	August 10, 2001
First Named Inventor	GEISTLICH et al.
Examiner Name	B.E. Pellegrino
Group Art Unit	3738
Attorney Docket Number	1194-179
Confirmation Number	5552

[X] Applicant claims small entity status

Total Amount of Payment ($)475.00

METHOD OF PAYMENT (check one)

1. [X] The Commissioner is hereby authorized to charge the fees indicated below or credit overpayment to Deposit Account Number 02-2135 in the name of Rothwell, Figg, Ernst & Manbeck

   [X] Charge any additional fee required under 37 CFR 1.16 and 1.17 to Deposit Account No. 02-2135.

2. [ ] Payment by check enclosed

FEE CALCULATION

1. FILING, SEARCH AND EXAMINATION FEES

Code	Fee	Fee Description	Fee Paid
1001	150	Utility Filing Fee	[ ]
	395	*filed before Dec. 8, 2004*	[ ]
1111	250	Utility Search Fee	[ ]
1311	100	Utility Examination Fee	[ ]
1002	100	Design Filing Fee	[ ]
	175	*filed before Dec. 8, 2004*	[ ]
1112	50	Design Search Fee	[ ]
1312	65	Design Examination Fee	[ ]
1003	100	Plant Filing Fee	[ ]
	275	*filed before Dec. 8, 2004*	[ ]
1113	150	Plant Search Fee	[ ]
1313	80	Plant Examination Fee	[ ]
1004	150	Reissue Filing Fee	[ ]
	395	*filed before Dec. 8, 2004*	[ ]
1114	250	Reissue Search Filing Fee	[ ]
1314	300	Reissue Examination Fee	[ ]
1005	100	Provisional Filing Fee	[ ]

SUBTOTAL $

2. CLAIMS

			Extra Claims		Fee	Fee Paid
Total Claims	[ ]	- 20* =	[ ]	x	$25 =	[ ]
Independent Claims	[ ]	- 3* =	[ ]	x	100 =	[ ]
Multiple Dependent Claims				+	180 =	[ ]

**or number previously paid, if greater*

SUBTOTAL $

3. APPLICATION SIZE FEE

Total Sheets [ ] - 100 = [ ]/50 = [ ]** x $125 =

*** Number of each additional 50 or fraction thereof*

SUBTOTAL $

FEE CALCULATION (continued)

4. ADDITIONAL FEES

Fee Code	Fee Paid	Fee Description	Fee Paid
1051	65	Surcharge - late filing fee or oath	[ ]
1052	50	Surcharge - late provisional filing fee or cover sheet	[ ]
1053	130	Non-English specification	[ ]
1812	2,520	For filing a request for reexamination	[ ]
1804	920	Requesting publication of SIR prior to Examiner action	[ ]
1805	1,840	Requesting publication of SIR after Examiner action (reduced by basic filing fee paid)	[ ]
1251	60	Extension for reply within first month	[ ]
1252	225	Extension for reply within second month	[225]
1253	510	Extension for reply within third month	[ ]
1254	795	Extension for reply within fourth month	[ ]
1255	1,080	Extension for reply within fifth month	[ ]
1401	250	Notice of Appeal	[ ]
1402	250	Filing a brief in support of an appeal	[250]
1403	500	Request for Oral Hearing	[ ]
1451	1,510	Petition to institute a public use proceeding	[ ]
1452	250	Petition to revive -unavoidable	[ ]
1453	750	Petition to revive - unintentional	[ ]
1807	50	Processing fee under 37 CFR 1.17(q)	[ ]
1806	180	Submission of Information Disclosure Statement	[ ]
1809	395	Filing a submission after final rejection (37 CFR .129(a))	[ ]
1810	395	For each additional invention to be examined (37 CFR 1.129(b))	[ ]
1801	395	Request for Continued Examination (RCE)	[ ]
1802	900	Request for expedited examination of a design application	[ ]
1504	300	Publication fee for early, voluntary, or normal publication	[ ]
1505	300	Publication fee for republication	[ ]
1455	200	Filing application for patent term adjustment	[ ]
1456	400	Request for reinstatement of term reduced	[ ]
1814	65	Statutory Disclaimer	[ ]
Other fee (specify)			[ ]

SUBTOTAL $475

SUBMITTED BY				Complete (if applicable)	
NAME AND REG. NUMBER	Patrick T. Skacel, Reg. No. 47,948				
SIGNATURE		DATE	April 19, 2006	DEPOSIT ACCOUNT USER ID	02-2135